ChemComm

Carbon dioxide gas accelerates solventless synthesis†

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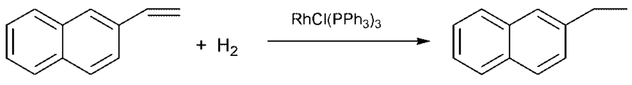
Received (in Covallis, OR, USA) 8th December 1999, Accepted 8th March 2000
Published on the Web 30th March 2000

Some solventless reactions involving solid reactants or products can be accelerated by the influence of subcritical gaseous CO_2.

Although the utility of supercritical carbon dioxide for solventless synthesis has been well publicized,[1] it is less well known that *subcritical gaseous* CO_2 can promote such reactions. At temperatures above 31 °C and pressures below 74 bar, carbon dioxide exists as a gas and not a supercritical fluid. It therefore does not dissolve organic solids or liquids to a significant extent. However, it is capable of dissolving *into* organics, and in so doing can affect the properties of the organic material such as its viscosity, diffusion coefficient,[2] dielectric constant, melting point,[3] glass transition temperature,[4] or ability to dissolve hydrogen.[5] In each of these ways, the presence of gaseous CO_2 could affect a reaction taking place in the organic phase. These possibilities have not been much explored. We now present examples of the effect of gaseous CO_2 on reactions involving organic solids.

Three reactions are offered as examples of the accelerating effect of CO_2. In each case, the reaction performance under gaseous CO_2 is compared to the performance in the absence of CO_2. In the first example, the starting material is a solid at the reaction temperature, while the product is a liquid. In the second example, the product is the solid. In the last example, both the starting material and the product are solids.

The first example is the hydrogenation of 2-vinylnaphthalene (lit.[6] mp 65–66 °C, mp of commercially available sample 62–65 °C) catalysed by $RhCl(PPh_3)_3$ (Scheme 1). In the absence of CO_2, this reaction can be performed at temperatures of 36 °C or higher (entry 4 in Table 1). The fact that it can proceed at temperatures somewhat below the melting point of 2-vinylnaphthalene is probably a result of a slow surface reaction generating a small quantity of the product, 2-ethylnaphthalene (mp −7.4 °C),[7] which acts as a liquid solvent for further reaction. Thus one would expect the reaction to proceed very slowly until enough liquid product has formed, at which point the system would accelerate. However, at 33 °C no conversion is observed in 30 min (entry 1).



Scheme 1

Table 1 Hydrogenation of 2-vinylnaphthalene in the absence of added solvent[a]

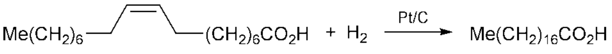
Entry	T/°C	P_{CO_2}[b]/bar	t/h	Conv. (%)	TOF[c]/h^{-1}
1	33	0	0.5	0	0
2	33	56	0.5	52[d]	310
3	33	0[e]	0.5	16	96
4	36	0	0.5	5[d]	33
5	36	56	0.5	73[d]	430
6	36	56	1.5	100	200

[a] 7 mg (7.6 μmol) $RhCl(PPh_3)_3$, 350 mg (2.27 mmol) 2-vinylnaphthalene, 10 bar H_2, vessel size 160 mL. [b] Calculated as $P_{total} - P_{H_2}$. [c] Turnover frequency = mol product per mol catalyst per hour. [d] Average of two runs. [e] H_2 pressure 66 bar.

In the presence of subcritical gaseous CO_2, the reaction proceeds more rapidly.† At 36 °C, the enhancement of the rate over that observed in the absence of CO_2 is at least an order of magnitude (entries 4 and 5). Complete conversion is obtained within 90 min (entry 6). At 33 °C, the yield after 30 min is obviously superior to that in the absence of CO_2 (compare entries 1 and 2). Hydrogen gas seems to be less effective than CO_2 in enhancing the rate (entry 3). Note that in all of the experiments, the pressure of CO_2 (56 bar) is below the critical pressure of CO_2 (73.9 bar),[8] while the total pressure of the H_2/CO_2 mixture (P_{tot} = 66 bar) is below the mixture critical pressure.‡ Thus one can be certain that the gaseous phase is not supercritical. It is unlikely that the reaction takes place in the gaseous phase because: (a) at the pressure used, the density of the gaseous CO_2 is so low (*ca.* 0.14 g mL^{-1} at 36 °C and 56 bar of CO_2)[8] that it can dissolve neither the substrate nor catalyst to any significant extent, (b) the catalyst used here has not been modified to render it soluble in CO_2, and (c) all of the product mixture was found inside the glass liner at the end of the reaction. The most likely explanation of the rate enhancement is the effect of gaseous CO_2 on the melting point of 2-vinylnaphthalene.

This explanation involves the phenomenon of gas-induced melting (or gas-induced melting point lowering) of organic solids. Melting of a solid compound A can not normally be achieved below the temperature of its triple point. However, in the presence of a gas B, the melting temperature of A becomes a function of the pressure of B. The melting temperature of A can be significantly lowered from its triple point, especially at pressures approaching the critical pressure of gas B. The degree of melting point lowering depends on the solubility of B in molten A, and can be limited by the occurrence of a critical end point in the binary phase diagram.§ The end result of this phase behaviour is that solid organic compounds can be made to melt even at temperatures well below their normal melting points. This phenomenon is the basis of the recently-developed PGSS (Particles from Gas Saturated Solution) process for the micronization of solids.[9–11] Note, however, that this effect alone can not bring the melting point of 2-vinylnaphthalene to as low as 36 or 33 °C; a combination of the induced-melting effect and some initial surface reaction is required to explain the rapid rate at these temperatures.

The hydrogenation of oleic acid to stearic acid, catalysed by 5% Pt/C (Scheme 2), is also affected by the induced-melting effect. Oleic acid is a model compound for the unsaturated fatty acids in vegetable oils.[12] While oleic acid is a liquid (mp 13–16 °C),[13] the hydrogenation product stearic acid (mp 69–70 °C)[14] is a solid at room temperature. Therefore, one would expect that the solventless hydrogenation would proceed



Scheme 2

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† Electronic supplementary information (ESI) available: experimental procedures for the hydrogenation of 2-vinylnaphthalene and oleic acid, and the hydroformylation of 2-vinylnaphthalene See http://www.rsc.org/suppdata/cc/a9/a909703a/

DOI: 10.1039/a909703a

Table 2 Hydrogenation of oleic acid in the absence of added solvent[a]

			Conv. (%)	
Entry	T/°C	t/h	P_{CO_2} = 0 bar	P_{CO_2} = 60 bar
1	35	1	90	97
2	35	4	90	97
3	35	25	90	—
4	50	1	94	98
5	50	4	95	99
6	50	25	95	—

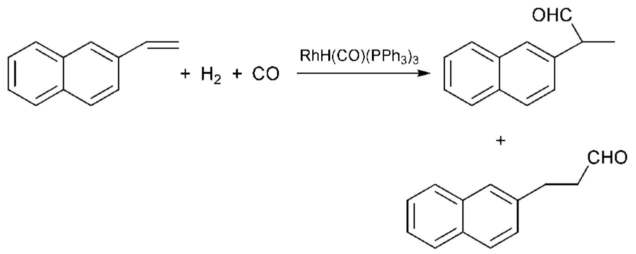
[a] 100 mg (0.35 mmol) oleic acid, 3.5 μmol Pt (as 5% Pt/C), 10 bar H_2, vessel size 160 mL, vial diameter 12 mm. P_{CO_2} calculated as $P_{total} - P_{H_2}$.

readily at temperatures above 4 °C, but the reaction should stop short of completion because at high conversions the melting point of the reaction mixture would climb above the ambient temperature; the conversion at which the reaction ‘stalls’ should be a function of the reaction temperature. At 50 °C, for example, the conversion climbs no higher than 95% even after 25 h (Table 2). The reaction in the presence of subcritical gaseous CO_2 attains 99% conversion within 4 h.† At 35 °C, the reaction in the absence of CO_2 climbs no higher than 90% even after 25 h, while it reaches 97% after 1 h in the presence of CO_2. Thus gaseous CO_2 has a strong effect on this reaction at high conversions.

The third reaction to be described is the solventless hydroformylation of 2-vinylnaphthalene catalysed by $RhH(CO)(PPh_3)_3$ (Scheme 3). This reaction generates 2-(2-naphthyl)propanal (mp 53 °C),[15] plus traces of 3-(2-naphthyl)propanal (mp 42 °C).[16] In the absence of CO_2, the melting point of the reaction mixture starts at 65 °C (the melting point of 2-vinylnaphthalene), drops after partial conversion (because a mixture forms), and rises up towards the melting point of the product as the reaction approaches completion. Thus in the absence of CO_2 and at temperatures below 50 °C, one would predict that the reaction would start slowly, accelerate after some product is formed, and become slow again at high conversions. Indeed, the presence of subcritical gaseous CO_2 was found to make the reaction start more quickly (Table 3, entries 1, 2, and 4) and reach completion more readily (entries 6–8).†

There are many advantages to performing a reaction by induced-melting rather than in a SCF: (1) the pressure of the SCF/gas is lower, (2) the volume of vessel required is lower, (3) the concentration of reagent in the reaction phase is much higher, which could lead to greater rates, (4) homogeneous catalysts do not have to be designed to be CO_2-soluble, and (5) depending on the substrate, the polarity of the reaction phase may be much higher than the very low polarity of $scCO_2$. The disadvantage of the induced-melting option is that it is only effective for organic solids which have melting points within 30–40 °C of the reaction temperature. Even for those reactions, one could perform the reaction by melting the reagent in the usual manner of raising the temperature, but this may not always be an option, depending on the temperature dependence of the selectivity (particularly for enantioselective reactions).

In conclusion, we have demonstrated, with three examples, the acceleration of solventless synthesis by the application of subcritical (gaseous) CO_2. The hydrogenation and hydroformylation reactions of 2-vinylnaphthalene are accelerated by CO_2 pressure, while the conversions obtained from the hydrogenation of oleic acid and hydroformylation of 2-vinylnaphthalene are improved by CO_2 pressure. The use of gaseous CO_2 can thus extend the range of temperatures at which ‘neat’ reactions can be performed. Future work will include the testing of other gases and other reactions.



Scheme 3

Table 3 Hydroformylation of 2-vinylnaphthalene in the absence of added solvent.[a]

			Conv. (%)	
Entry	T/°C	t/h	P_{CO_2} = 0 bar	P_{CO_2} = 55 bar
1	33	0.5	0	8.5
2	33	2	9.6	24
3	33	16	—	88
4	36	2	14	44
5	43	1	—	74
6	43	2	93	96
7	43	4	—	100
8	43	11	98	—

[a] 12 mg (13 μmol) $RhH(CO)(PPh_3)_3$, 400 mg (2.6 mmol) 2-vinylnaphthalene, 10 bar each of CO and H_2, vessel size 160 mL, vial diameter 22 mm. P_{CO_2} calculated as $P_{total} - P_{H_2} - P_{CO}$. The selectivity of the reaction is high (14 : 1) for the desired[17] branched aldehyde.

This material is based upon work supported by the EPA/NSF Partnership for Environmental Research under NSF Grant No. 9815320. We also acknowledge useful discussions with Dr Charles Eckert of the Georgia Institute of Technology and experimental assistance from Mr Philip Stalcup.

Notes and references

‡ The mixture critical pressure curve starts at 73.9 bar for pure CO_2 and rises with increasing H_2 mol fraction.[18]

§ Not all binary solid/SCF mixtures have such an end point. For example, the systems *p*-dichlorobenzene/ethene and menthol/ethene do not. In these systems, the induced lowering of the melting temperature can be significantly greater: G. A. M. Diepen and S. E. C. Scheffer, *J. Am. Chem. Soc.*, 1948, **70**, 4081.

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